

## Safety Data Sheet



Bristol-Myers Squibb Company

<b>1. IDENTIFICATION</b>													
<i>Product Information</i>													
Product name	ELIQUIS® (apixaban) Film-Coated Tablets, 2.5 mg & 5.0 mg												
Version	2.0, 29.11.2017												
Jurisdiction	This Safety Data Sheet was prepared in accordance with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) for the United States of America (USA) (CFR 1910.1200), European Union (EU) (EC 1272/2008) and United Nations (UN). The following countries utilize the UN GHS classification process: Mexico, Brazil, China, New Zealand, Canada, Japan, and Korea.												
Active substance	Apixaban												
Synonyms	BMS-562247-01 Tablets; BMS 562247-01 Tablets; AG0023 Tablets; DPH-150123 Tablets; Apixaban Tablets; Apixaban												
Other information	Project Name: 020F6												
Intended Uses	This material is a finished drug product for patient use. It is used as an anticoagulant. Non-intended uses such as crushing or grinding of tablets should be avoided to prevent the generation of dust.												
<i>Company/Undertaking Identification</i>													
Address	<table style="width: 100%; border: none;"> <tr> <td style="width: 33%;"><u>USA</u></td> <td style="width: 33%;"><u>Ireland</u></td> </tr> <tr> <td><b>Bristol-Myers Squibb Company</b></td> <td><b>Bristol-Myers Squibb Company</b></td> </tr> <tr> <td>P.O. Box 191</td> <td>Swords Laboratories, Watery Lane</td> </tr> <tr> <td>New Brunswick, New Jersey 08903</td> <td>Swords, Ireland</td> </tr> <tr> <td>United States of America</td> <td>MG-GBS-MSDS-Request@bms.com</td> </tr> <tr> <td>1-800-332-2056</td> <td>353-1813-9456</td> </tr> </table>	<u>USA</u>	<u>Ireland</u>	<b>Bristol-Myers Squibb Company</b>	<b>Bristol-Myers Squibb Company</b>	P.O. Box 191	Swords Laboratories, Watery Lane	New Brunswick, New Jersey 08903	Swords, Ireland	United States of America	MG-GBS-MSDS-Request@bms.com	1-800-332-2056	353-1813-9456
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Emergency Phone No.	<table style="width: 100%; border: none;"> <tr> <td style="width: 33%;">USA (also Canada, Puerto Rico and the Virgin Island): 1-800-424-9300</td> <td style="width: 33%;"><u>Ireland</u>: 353-1813-9456</td> </tr> <tr> <td colspan="2">Other Countries: See "Section 16" for country-specific emergency phone numbers from CHEMTREC.</td> </tr> </table>	USA (also Canada, Puerto Rico and the Virgin Island): 1-800-424-9300	<u>Ireland</u> : 353-1813-9456	Other Countries: See "Section 16" for country-specific emergency phone numbers from CHEMTREC.									
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Other Countries: See "Section 16" for country-specific emergency phone numbers from CHEMTREC.													

<b>2. HAZARDS IDENTIFICATION</b>	
<b>Classification and Labelling Common to All Jurisdictions</b>	
Classification	Serious Eye Damage/Eye Irritation - Category 2 Specific Target Organ Systemic Toxicity (Single Exposure) - Category 3
Symbol	
Hazard Statements	Causes serious eye irritation. May cause respiratory irritation .
Precautionary Statements	Wash thoroughly after handling. Wear protective gloves/clothing and eye/face protection. Use only outdoors or in a well-ventilated area.

<b>2. HAZARDS IDENTIFICATION</b>	
<b>Classification and Labelling for Specific Jurisdictions</b>	
<b>USA</b>	
Classification	Specific Target Organ Systemic Toxicity (Repeated Exposure) - Category 1
Signal Word	Danger
Hazard Statements	Causes damage to organs (blood) through prolonged or repeated exposure.
Precautionary Statements	Do not breathe dust. Do not eat, drink or smoke when using this product.
<b>EU</b>	
Classification	Specific Target Organ Systemic Toxicity (Repeated Exposure) - Category 2
Signal Word	Warning
Hazard Statements	May cause damage to organs (blood) through prolonged or repeated exposure.
Precautionary Statements	Do not breathe dust.
<b>UN</b>	
Classification	Specific Target Organ Systemic Toxicity (Repeated Exposure) - Category 1
Signal Word	Danger
Hazard Statements	Causes damage to organs (blood) through prolonged or repeated exposure.
Precautionary Statements	Do not breathe dust. Do not eat, drink or smoke when using this product.
Other information	56% of the mixture consists of ingredient(s) of unknown hazards to the aquatic environment.

<b>3. COMPOSITION/INFORMATION ON INGREDIENTS</b>					
Components	Concentration	CAS No.	EU only		Other Registration No.
			EC No./REACH Registration No.	H-code(s)	
<i>Hazardous components</i> Apixaban	2.4 %	Trade Secret	--	H372	--
Microcrystalline Cellulose	< 40 %	9004-34-6	232-674-9	H335	--
Sodium Lauryl Sulfate	< 1 %	151-21-3	205-788-1	H302	--

				H311 H315 H318 H335 H412	
Magnesium Stearate	< 5 %	557-04-0	209-150-3	--	--
<i>Other ingredients</i>					
Non-Hazardous Ingredients	< 50 %	Not available	--	--	--
See section 16 for H-code text.					

#### **4. FIRST AID MEASURES**

Eye contact	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists, get medical advice/attention. Keep eye wide open while rinsing.
Skin contact	Take off contaminated clothing and shoes immediately. Wash off immediately with plenty of water for at least 15 minutes. Discard contaminated clothing or wash before re-use. Get medical attention/advice if you feel unwell.
Inhalation	IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing. Call a POISON CENTER or doctor/physician if you feel unwell. Oxygen or artificial respiration if needed.
Ingestion	Do NOT induce vomiting. Never give anything by mouth to an unconscious person. Get medical attention/advice if you feel unwell.
Notes to Physician	This product has been reported to interact with the following medications: drugs that inhibit cytochrome P-450. Anticoagulants may cause increased bleeding during childbirth. Refer to Section 11.
Medical Surveillance	The need for a pre-placement, follow-up physical examination and history for employees with potential exposure to this compound is to be evaluated by a physician that is thoroughly knowledgeable about both the toxicity of this compound and the extent of work place exposure. Baseline testing would include: a medical history with emphasis on unusual bleeding, a complete blood count with differential. Based on opportunity for exposure and duration of exposure a periodic follow-up examination may be considered. It is recommended that the content be similar to the pre-placement exam. Employees who are pregnant, are breast-feeding, or who are concerned with other reproductive issues should be encouraged to consult with the occupational health physician monitoring worker's health.

#### **5. FIRE-FIGHTING MEASURES**

Flammable Properties	Not available
Extinguishing Media	Suitable extinguishing media: Dry chemical, Water spray, Foam Unsuitable extinguishing media: Do NOT use water jet.
Protection of Firefighters	Specific hazards: Not available Protective equipment: Use personal protective equipment. In the event of fire, wear self-contained breathing apparatus. Hazardous Combustion Products: carbon oxides (COx), nitrogen oxides (NOx), and, sulphur compounds
Other information	Decontaminate protective clothing and equipment before reuse.

**6. ACCIDENTAL RELEASE MEASURES**

Personal precautions	Refer to protective measures listed in sections 7 and 8. Use personal protective equipment. Examples include tightly fitting safety goggles, lab coat and impervious gloves. Wear respiratory protection. Depending on the nature of the spill (quantity and extent of spill) additional protective clothing and equipment such as a self-contained breathing apparatus may be needed.
Environmental precautions	Prevent release to drains and waterways. Prevent release to the environment.
Containment Methods	Wet down any dust to prevent generation of aerosols, if appropriate. Cover with suitable material.
Cleanup Methods	Contain and collect spillage and place in container for disposal according to local regulations (see Section 13). Handle waste materials, including gloves, protective clothing, contaminated spill cleanup material, etc., as appropriate for chemically and pharmacologically similar materials.

**7. HANDLING AND STORAGE**

Handling Precautions	Avoid exposure - obtain special instructions before use. Avoid formation of dust and aerosols. When handling broken or crushed tablets or capsules, ensure worker exposure is below the recommended exposure limit. Keep away from heat and sources of ignition. Prevent release to drains and waterways. Use only outdoors or in a well-ventilated area.
Container Requirements	Store in the original primary packaging as provided. Keep container tightly closed.
Storage Conditions	Store in well-ventilated place. Keep container tightly closed. Store at room temperature. Protect against light. Keep away from heat, sparks and flames. Store locked up.
Specific use(s)	Refer to Section 1

**8. EXPOSURE CONTROLS / PERSONAL PROTECTION**

Exposure limit(s)	Company Guideline	ACGIH	Germany OEL	UK MEL
Apixaban	3 µg/m <sup>3</sup> 8 hour-TWA	--	--	--
Microcrystalline Cellulose		10 mg/m <sup>3</sup> TWA	--	--
Magnesium Stearate		10 mg/m <sup>3</sup> 8 hour-TWA	--	--
Microcrystalline Cellulose	Occupational Exposure Limits have been established by: - Belgium - Switzerland - Estonia - Spain - France - Ireland - Portugal - Latvia			
Magnesium Stearate	Occupational Exposure Limits have been established by: - Belgium - Spain - Ireland - Portugal - Sweden			

**8. EXPOSURE CONTROLS / PERSONAL PROTECTION**

Recommended Industrial Hygiene Monitoring Methods	Contact the Bristol-Myers Squibb AIHA accredited Industrial Hygiene Laboratory at (USA) 732-227-6338.  General - The health hazard risk of handling this material is dependent on many factors, including physical form, % API in material being handled, duration and frequency of process task, and effectiveness of controls. If it is necessary to handle this compound outside of engineering controls, an exposure risk assessment should be conducted and procedures documented by a qualified EHS professional. See Section 4 "Notes to Physician" for information on medical surveillance.
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**EXPOSURE CONTROLS / PERSONAL PROTECTION FOR MATERIAL AS SUPPLIED**

This formulation contains an active pharmaceutical ingredient (API) with the guideline limit noted above. To keep the API below the recommended guideline, the material as supplied should be controlled during handling to limit total airborne aerosol exposure to: 125 µg/m<sup>3</sup> (Material is assigned to Exposure Control Band 2 (range 100 - 1000 µg/m<sup>3</sup>)).

Engineering Controls and Ventilation	FOR MANUFACTURING PROCESSES (BULK): Use process enclosures, containment technology, or other engineering controls to keep airborne levels below recommended exposure limit. When handling quantities up to 150 milligrams, a standard laboratory with general laboratory dilution ventilation (e.g. 6-12 air changes per hour) is appropriate. When handling quantities from 150 milligrams to 1 kilogram, work in a standard laboratory using a fume hood; biological safety cabinet(Class II, all types), approved vented enclosure; specific local exhaust. Quantities exceeding 1 kilogram should be handled in a designated laboratory. A laminar flow/powder containment booth is recommended for handling >1 kilograms of active substance. For manufacturing and pilot plant operations, use semi to closed material transfer systems and containment of open operations. HEPA filtration for recirculation of exhaust is required.  FOR CLINICAL SETTING USE (DRUG PRODUCT): When handling small quantities in a clinical setting, good room ventilation is desirable. Specific engineering controls should not be needed.
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Respiratory protection	Use and selection of respiratory protection is based upon engineering controls in use and potential for aerosol generation. When engineering controls are not sufficient control exposure, wear an approved respirator with NIOSH Class 100 or high efficiency particulate (HEPA) filters or cartridges (EN 140/EN 136) when exposures are up to 10 times the exposure control guideline. Wear a loose-fitting (Tyvek or helmet type) HEPA powered-air purifying respirator (PAPR) (EN 12941) when exposures are 10-25 times the exposure control guideline. Wear a full facepiece negative pressure respirator with Class 100 or HEPA filters (EN 136) when exposures are 25-50 times the exposure control guideline. Wear a tight-fitting, full facepiece HEPA PAPR (EN 12942) when exposures are 50-100 times the exposure control guideline. Wear a hood-shroud HEPA PAPR (EN 12941) or full facepiece supplied air respirator (EN 139) operated in a pressure demand or other positive pressure mode when exposures are 100-1000 times the exposure control guideline.
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Eye protection	Safety glasses with side-shields are recommended (EN 166). Face shields or chemical safety goggles (EN 166) may be required if splash potential exists or if corrosive materials are present. Note: Choice of eye protection may be influenced by the type of respirator which is selected.
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Hand protection	Impervious nitrile, rubber and latex gloves are recommended (EN 420, EN 374). If material is handled in solution, the solvent should also be considered when selecting protective clothing material. Please note that employees who are allergic to natural rubber latex should use nitrile gloves.
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**8. EXPOSURE CONTROLS / PERSONAL PROTECTION**

Skin and body protection	FOR MANUFACTURING PROCESSES (BULK): Wear a laboratory coat (EN 340) when handling quantities up to 1 kilograms. For quantities over 1 kilogram, wear laboratory coat (EN 340) or coverall of low permeability (EN 1149-1). For manufacturing operations, wear coverall of low permeability (EN 1149-1). FOR CLINICAL SETTING USE (DRUG PRODUCT): When handling small quantities in a clinical setting, good room ventilation is desirable. Specific engineering controls should not be needed.
Hygiene	Wash hands and face before breaks and immediately after handling the product.
Environmental exposure controls	Prevent release to drains and waterways.

**9. PHYSICAL AND CHEMICAL PROPERTIES**

<i>General Information</i>	
<i>Appearance</i>	
Physical State	solid
Color	yellow pink brown or white to off-white
Form	tablet
<i>Odour</i>	
Odour	Not available
Odor Threshold	Not available
pH	Not available
<i>Other information</i>	
Bulk density	Not available
Evaporation rate	Not available
Molecular formula	Not applicable
Hydrolysis/Photolysis	Not available
Hygroscopicity	Not available
Molecular Weight	Not applicable
Log Octanol/Water Partition Coefficient [log Kow]	Not available
Surface Tension	Not available
pKa	Not available
Particle Size	Not available
Solubility, Water	Not available
Specific Gravity/ Relative density	Not available
Viscosity, dynamic	Not available
Viscosity, kinematic	Not available
% Volatile	Not available
<i>Thermal/Stability properties</i>	
Autoignition temperature	Not available
Boiling Point	Not available
Thermal decomposition	Not available
Explosive Limits, LEL	Not available
Explosive limits, UEL	Not available
Explosiveness	Not available
Flammability	Not available

**9. PHYSICAL AND CHEMICAL PROPERTIES**

Flash point	Not available
Melting Point	Not available
Oxidizing Potential	Not available

*Vapor Properties*

Vapor Density	Not available
Vapor Pressure	Not available
Saturated Vapor Concentration	Not available

**10. STABILITY AND REACTIVITY**

*Stability*

Chemical Stability	Stable under normal conditions.
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Conditions to avoid	Not available
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Materials to avoid	Not available
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Hazardous decomposition products	Hazardous decomposition products formed under fire conditions.: carbon oxides (COx), nitrogen oxides (NOx), and, sulphur compounds
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Hazardous reactions	None known.
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*Sensitivity to static discharge/Dust exp.*

Summary Statements	Although material has not been specifically tested, fine dust suspended in air in sufficient concentration and in the presence of an ignition source may pose a potential explosion hazard. Provide appropriate bonding and grounding protection to control static charge. Powder handling equipment such as dust collectors, dryers, and mills may require additional protective measures (e.g. explosion venting, inerting, etc.).
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**11. TOXICOLOGICAL INFORMATION**

Routes of Entry	Ingestion, inhalation, Eye contact, Skin contact
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Eye Irritation	<u>Apixaban</u> Not an eye irritant based on in vitro assay
	<u>Microcrystalline Cellulose</u> Mildly and/or transiently irritating to eyes
	<u>Sodium Lauryl Sulfate</u> Severely irritating to eyes.
	<u>Magnesium Stearate</u> May cause mechanical irritation.

Skin Irritation	<u>Apixaban</u> Not irritating to skin.
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## 11. TOXICOLOGICAL INFORMATION

Microcrystalline Cellulose

Not irritating to skin.

Sodium Lauryl Sulfate

Irritating to skin.

Magnesium Stearate

Not irritating to skin.

Respiratory Irritation

Microcrystalline Cellulose

Irritating to respiratory tract.

Sodium Lauryl Sulfate

Irritating to respiratory tract.

Magnesium Stearate

Mildly and/or transiently irritating to respiratory tract.

Sensitization

Apixaban

Not a dermal sensitizer in an experimental study

Microcrystalline Cellulose

Not a dermal sensitizer

Sodium Lauryl Sulfate

Allergic contact dermatitis is quite rare but has been reported.

Acute Toxicity Study

**Acute Oral**

Apixaban

LD50 (rat, males and females): > 4,510 mg/kg

LD50 (mouse, males and females): > 4,000 mg/kg

Minimum lethal dose (monkey, males and females): 100 mg/kg Hemorrhaging was considered secondary to inadvertent arterial puncture in association with drug treatment.

LD50 (dog, females): > 1,500 mg/kg No mortality occurred.

Microcrystalline Cellulose

LD50 (rat, males and females): > 5,000 mg/kg

Sodium Lauryl Sulfate

LD50 (rat): 1,288 mg/kg

Magnesium Stearate

LD50 (rat): > 10,000 mg/kg

**Acute Dermal**

Microcrystalline Cellulose

LD50 (rat, males and females): > 2,000 mg/kg

Sodium Lauryl Sulfate



## 11. TOXICOLOGICAL INFORMATION

LD50 (rat): > 2,000 mg/kg  
LD50 (rabbit): 580 mg/kg  
LD50 (guinea pig): 1,200 - 2,000 mg/kg

### Acute inhalation toxicity

#### Microcrystalline Cellulose

LC50 (rat, males and females): > 5350 mg/m<sup>3</sup>/4 H

#### Sodium Lauryl Sulfate

LC50 (rat): > 3,900 mg/m<sup>3</sup>/1hr/1 H

#### Magnesium Stearate

LC50 (rat): > 2,000 mg/l/1 H

### Acute toxicity (other routes of administration)

#### Apixaban

LD50 (mouse, males and females, intravenous): 50 mg/kg

LD50 (rat, intravenous): > 25 mg/kg

#### Microcrystalline Cellulose

LD50 (rat, males, intraperitoneal): > 3,150 mg/kg

### Repeated Dose Toxicity

#### Apixaban

2 - 104 weeks oral (daily) mouse, rat, dog study (males and females): NOAEL (3 month, dog) = 5 mg/kg; Low dose effects include (<= 100 mg/kg): minimal changes in clinical chemistry parameters, changes in blood clotting parameters. High dose microscopic effects include: lymph nodes. After recovery, all parameters returned to normal.

2 Weeks intravenous (daily) rat, dog study (males and females): NOAEL (2 week, dog) = 0.4 mg/kg; Low dose effects include (<= 100 mg/kg): minimal changes in clinical chemistry parameters, changes in blood clotting parameters.

#### Sodium Lauryl Sulfate

2 Years dietary (daily) rat study: NOAEL = 1%; No significant adverse effects were observed.

#### Magnesium Stearate

3 months dietary rat study: NOAEL = 2,500 mg/kg; Low dose effects include (<= 100 mg/kg): decreased weight gain, liver effects, kidney stones.

### Genetic Toxicity

#### Apixaban

##### **Mutagenicity Assessment**

This material was negative in a battery of in vivo and in vitro genotoxicity assays.

#### Microcrystalline Cellulose

##### **Mutagenicity Assessment**

This material was negative in a battery of in vivo and in vitro genotoxicity assays.

#### Sodium Lauryl Sulfate

##### **Mutagenicity Assessment**

**11. TOXICOLOGICAL INFORMATION**

Several studies were conducted. This material was negative in a battery of in vivo and in vitro genotoxicity assays.

Magnesium Stearate

**In vitro**

Ames reverse-mutation assay --  
negative

**Carcinogenicity**

Apixaban

104 Weeks dietary (daily) rat study : Tumor NOAEL = 600 mg/kg (males and females). No treatment-related tumors were observed.  
104 Weeks dietary (daily) mouse study : Tumor NOAEL = 1,500 mg/kg (males). No treatment-related tumors were observed.

**Carcinogenicity Assessment**

This material did not show carcinogenic potential in animal studies.

Microcrystalline Cellulose

**Carcinogenicity Assessment**

This material did not show carcinogenic potential in animal studies. Not classifiable as to its carcinogenicity to humans.

Sodium Lauryl Sulfate

**Carcinogenicity Assessment**

This material did not show carcinogenic potential in animal studies.

Magnesium Stearate

**Carcinogenicity Assessment**

Not classifiable as to its carcinogenicity to humans.

<b>Carcinogenicity</b>	<b>ACGIH</b>	<b>IARC</b>	<b>NTP</b>
Apixaban	--	--	--
Microcrystalline Cellulose	--	--	--
Sodium Lauryl Sulfate	--	--	--
Magnesium Stearate	A4	--	--

**Reproductive Toxicity**

Apixaban

oral (daily) Study of Fertility and Early Embryonic Development (rat) (males and females) LOAEL = 50 mg/kg  
Effects include: changes in blood clotting parameters. No effects were found on mating or fertility.

**Assessment Reproductive Toxicity**

Data indicate that this compound is not a reproductive hazard.

Microcrystalline Cellulose

**Assessment Reproductive Toxicity**

Data indicate that this compound is not a reproductive hazard.

**Developmental Toxicity**

Apixaban

oral (daily) Study of Embryo-Fetal Development (mouse) (parent, females) LOAEL = 600 mg/kg

**11. TOXICOLOGICAL INFORMATION**

(embryo/fetus) NOAEL = 1500 mg/kg  
Maternal effects include: changes in blood clotting parameters. No effects were observed in the fetus/embryo.

oral (daily) Study of Embryo-Fetal Development (rat)  
(parent, females) LOAEL = 100 mg/kg  
(embryo/fetus) NOAEL = 3000 mg/kg  
Maternal effects include: vaginal discharge, fecal changes. No effects were observed in the fetus/embryo.

oral Study of Embryo-Fetal Development (rabbit)  
(parent, females) NOAEL = 1500 mg/kg  
(embryo/fetus) NOAEL = 1500 mg/kg  
No significant adverse effects were observed.

intravenous Study of Embryo-Fetal Development (rabbit)  
(parent, females) LOAEL = 1.25 mg/kg  
(embryo/fetus) NOAEL = 5 mg/kg  
Maternal effects include: damage at injection sites, changes in blood clotting parameters. No effects were observed in the fetus/embryo.

oral Study of Pre- and Postnatal Development (rat)  
(parent, females) LOEL = 25 mg/kg  
(F1 offspring) NOAEL = 25 mg/kg  
Offspring effects include: decreased fertility. Maternal effects include: changes in blood clotting parameters.

**Developmental Toxicity Assessment**

No significant adverse effects were observed. Anticoagulants may cause increased bleeding during childbirth.

Microcrystalline Cellulose

**Developmental Toxicity Assessment**

Available data do not indicate a potential for selective developmental toxicity.

Sodium Lauryl Sulfate

**Developmental Toxicity Assessment**

Adverse effects on the fetus occur only at doses that also cause maternal toxicity.

Human experience

**Experiences with Human Exposure**

Apixaban

oral Clinical trial(s) low exposure - acute effects include: headache, dizziness, bleeding, bruising, blood in stool, bloody urine, gastrointestinal tract disorders, anemia, rash, changes in blood clotting parameters, changes in clinical chemistry parameters. low exposure - long term exposure effects include: fever, cerebral bleeding.

Target Organs

Apixaban  
blood

Symptoms

Apixaban  
See "Human Experience".

Microcrystalline Cellulose

**11. TOXICOLOGICAL INFORMATION**

labored respiration, noisy respiration, chest pain, breathing difficulties, shortness of breath, lung inflammation

Sodium Lauryl Sulfate

redness and swelling of skin and eyes, pain, tissue destruction, blindness, labored respiration, noisy respiration, chest pain, breathing difficulties, shortness of breath, lung inflammation

Magnesium Stearate

redness and swelling of eyes, skin flushing, nausea, vomiting, diarrhoea, dehydration, lowered blood pressure, cardiac irregularities, CNS depression, respiratory disorder, paralysis

Pharmacokinetics/  
Toxicokinetics

Apixaban

Absorption: Data available upon request.

Distribution: Data available upon request.

Metabolism: Data available upon request.

Elimination: Half-life = 12 Hour(s) (Human). Data available upon request.

Other Toxicity Information

**Other Toxicity Tests**

Apixaban

Telemetry Study (dog) : intravenous = 1.25 - 4 mg/kg No significant adverse effects were observed. No significant cardiovascular or hemodynamic effects noted.

Phototoxicity : In vitro = negative

## 12. ECOLOGICAL INFORMATION

### Ecotoxicity effects

#### **Acute Toxicity to Fish**

##### Apixaban

LC50 (fathead minnows ): > 25 mg/l. (limit of solubility)

##### Microcrystalline Cellulose

LC50 (Oncorhynchus mykiss (rainbow trout), 96 H): > 100 mg/l.

##### Sodium Lauryl Sulfate

LC50 (Pimephales promelas (fathead minnow), 96 H): 10.2 mg/l.

LC50 (Oncorhynchus mykiss (rainbow trout), 96 H): 4.6 mg/l.

#### **Acute Toxicity to Aquatic Invertebrates**

##### Apixaban

EC50 (Daphnia magna (Water flea)): > 24 mg/l. (limit of solubility)

##### Microcrystalline Cellulose

LC50 (Daphnia, 48 H): > 100 mg/l.

##### Sodium Lauryl Sulfate

EC50 (Daphnia, 48 H): 1.8 mg/l.

#### **Toxicity to aquatic plants**

##### Apixaban

EC50 (Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum)): > 23 mg/l (limit of solubility)

NOEC (Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum)): 3.6 mg/l

##### Microcrystalline Cellulose

EC50 (Algae, 96 H): > 100 mg/l

##### Sodium Lauryl Sulfate

EC50 (Scenedesmus subspicatus, 72 H): 53 mg/l

#### **Toxicity to microorganisms**

##### Apixaban

Respiration inhibition, EC50 : > 1,000 mg/l

##### Sodium Lauryl Sulfate

EC50 (Photobacterium phosphoreum, 5 Minute): 1.19 mg/l

#### **Chronic toxicity to fish**

##### Apixaban

LOEC (Pimephales promelas (fathead minnow)): > 10 mg/l

NOEC: 10 mg/l

##### Sodium Lauryl Sulfate

NOEC (Pimephales promelas (fathead minnow), 42 D): > 1.35 mg/l(limit of solubility)

#### **Chronic toxicity to aquatic invertebrates**

##### Apixaban

LOEC (Daphnia magna (Water flea)): 23 mg/l

NOEC (Daphnia magna (Water flea)): 9.6 mg/l

##### Sodium Lauryl Sulfate

NOEC (Daphnia, 7 D): 0.88 mg/l

#### **Toxicity to sediment/soil dwelling organisms**

##### Apixaban

LOEC (Chironomus sp. (midge)): > 100 mg/ml

### **Mobility**

Not available

### **Persistence and degradability**

#### **Biodegradation**

##### Apixaban

Ready biodegradation: 0 %; Not readily biodegradable.

##### Microcrystalline Cellulose

Inherently biodegradable - biodegrades in the environment.

##### Sodium Lauryl Sulfate

**12. ECOLOGICAL INFORMATION**

Biodegradation (28 D): 95.8 %; Readily biodegradable.

Apixaban

Koc (soil) : 12.2

**Bioaccumulative potential**

Apixaban

Log Octanol/Water Partition Coefficient [log Kow]: 1.20

**PBT and vPvB Assessment:**

Apixaban

Does not fulfill PBT or vPvB criteria

Microcrystalline Cellulose

Not available

Sodium Lauryl Sulfate

Not available

Magnesium Stearate

Not available

**13. DISPOSAL CONSIDERATIONS**

Advice On Disposal And Packaging

Disposal should be in accordance with applicable regional, national and local laws and regulations. Local regulations may be more stringent than regional or national requirements. This information presented only applies to the material as supplied.

Other information

This information presented only applies to the material as supplied.

**14. TRANSPORT INFORMATION**

This material is not a dangerous good for the purpose of transportation in all modes.

**15. REGULATORY INFORMATION**

**United States of America**

313 Toxic Release Inventory No components listed on the SARA 313 inventory.

TSCA Inventory Not listed. Food, drug and cosmetic products are exempt from TSCA.

**EU Regulation (EC) No 1272/2008)**

**DRUG PRODUCT**

Classification Medicinal products are exempt from classification and labeling requirements under EU Regulation (EC) No 1272/2008.

Regulatory Authorizations and Restrictions: Not available

**16. OTHER INFORMATION**

*Text of H-code(s) mentioned in Section 3.*

H302 Harmful if swallowed.

H311 Toxic in contact with skin.

H315 Causes skin irritation.  
 H318 Causes serious eye damage.  
 H335 May cause respiratory irritation  
 H372 Causes damage to organs through prolonged or repeated exposure.  
 H412 Harmful to aquatic life with long lasting effects.

*Recommended Restrictions for Use:*

Not available

*SDS preparation information*

Prepared by Global Environment, Health, Safety, and Sustainability 1-732-227-7380

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This Safety Data Sheet has been revised. This data sheet contains changes from the previous version in section(s): 2, 3, 4, 11, 15, and 16.

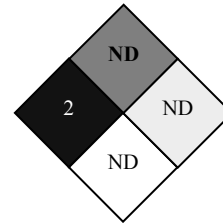
*Other information*

HMIS

Health	2*
Flammability	Not Determined (ND)
Reactivity	Not Determined (ND)
Personal protective equipment	See Section 8.

NFPA

Health 2  
 Fire ND  
 Reactivity ND  
 Special ND



*Country- Specific Emergency  
Phone Numbers*

<b>CHEMTREC</b> In-Country Dial Numbers	Local # Provided in Country	Toll Free in Country*	Greeting Language
CHEMTREC South Africa*		0-800-983-611	English
CHEMTREC Argentina (Buenos Aires)	+(54)-1159839431		Latin American Spanish
CHEMTREC Brazil (Rio De Janeiro)	+(55)-2139581449		Portuguese
CHEMTREC Chile (Santiago)	+(56)-25814934		Latin American Spanish
CHEMTREC Colombia *		01800-710-2151	Latin American Spanish
CHEMTREC Mexico*		01-800-681-9531	Latin American Spanish
CHEMTREC Peru (Lima)	+(51)-17071295		Latin American Spanish
CHEMTREC China*	4001-204937		Mandarin
CHEMTREC Hong Kong (Hong Kong)*		800-968-793	Cantonese
CHEMTREC India *		000-800-100-7141	Hindi
CHEMTREC Indonesia *		001-803-017-9114	Indonesian
CHEMTREC Japan (Tokyo)	+(81)-345209637		Japanese
CHEMTREC Malaysia *		1-800-815-308	Malay
CHEMTREC Philippines *		1-800-1-116-1020	Tagalog
CHEMTREC Singapore*		800-101-2201	Mandarin
CHEMTREC Singapore	+(65)-31581349		Mandarin
CHEMTREC South Korea*		00-308-13-2549	Korean
CHEMTREC Taiwan*		00801-14-8954	Mandarin
CHEMTREC Thailand *		001-800-13-203-9987	Thai
CHEMTREC Vietnam (Ho Chi Minh City)	+(84)-838012436		Vietnamese
CHEMTREC Australia (Sydney)	+(61)-290372994		English
CHEMTREC Belgium (Brussels)	+(32)-28083237		French and Flemish
CHEMTREC Czech Republic (Prague)	+(420)-228880039		Czech
CHEMTREC France	+(33)-975181407		French
CHEMTREC Germany *		0800-181-7059	German
CHEMTREC Hungary (Budapest)	+(36)-18088425		Hungarian
CHEMTREC Italy *		800-789-767	Italian
CHEMTREC Italy (Milan)	+(39)-0245557031		Italian
CHEMTREC Netherlands	+(31)-858880596		Dutch
CHEMTREC Poland (Warsaw)	+(48)-223988029		Polish
CHEMTREC Spain*		900-868538	European Spanish
CHEMTREC Sweden (Stockholm)	+(46)-852503403		Swedish
CHEMTREC Switzerland (Zurich)	+(41)-435016715		German
CHEMTREC UK (London)	+(44)-870-8200418		English
CHEMTREC Bahrain (Bahrain)	+(973)-16199372		Arabic
CHEMTREC Israel (Tel Aviv)	+(972)-37630639		Hebrew

\*Phone numbers for countries marked with an asterisk must be dialed within the country

The information contained in this SDS is believed to be accurate and represents the best information reasonably available at the time of preparation. However, we make no warranty, express or implied, with respect to such information, and we assume no liability from its use.